Lipoprotein Metabolism and Fattening in Poultry

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ABSTRACT   Because de novo fatty acid synthesis in birds takes place mainly in the liver, adipose tissue growth and subsequent fattening depend on the availability of plasma triglycerides, which are transported as components of lipoproteins. In growing birds, VLDL is the major transporter of triglycerides, and attempts to reduce excessive fatness in poultry have involved the control of VLDL metabolism. Lean and fat lines of chickens have been selected on the basis of either their abdominal fat content or plasma VLDL concentration. In both cases, hepatic lipogenesis or LPL activity in adipose tissue did not differ between lean and fat lines, and therefore they did not appear to be limiting factors of susceptibility to fattening. In contrast, hepatic secretion and plasma concentration of VLDL were always higher in fat chickens than in lean chickens. Thus, current methods of selection of broilers against excessive fatness are based on this direct relationship between plasma VLDL and adiposity. When hepatic lipogenesis exceeds the capacity of VLDL secretion, triglycerides accumulate in the liver, causing steatosis. Although fatty liver is associated with reduced egg production and increased mortality in laying hens, hepatic steatosis in overfed ducks and geese is of positive economic value, serving as the basis for “foie-gras” production. The balance between synthesis and secretion of VLDL is therefore the key point that regulates hepatic and extrahepatic fattening in poultry. J. Nutr. 127: 805S–808S, 1997.

KEY WORDS: chicken • geese • fattening • liver steatosis • VLDL

In avian species, lipids and especially triglycerides may be stored in adipocytes, hepatocytes and growing oocytes. Lipid storage in the latter is associated with vitellogenesis and further development of the embryo and will not be discussed in the present review. Excessive accumulation of lipids in the adipose tissue of modern lines of broilers is a major concern for producers, because most fat depots are lost during evisceration of the carcass or processing of the meat, which results in lower meat yields. Finally, hepatic steatosis must be avoided in laying hens but is of economic value in the overfed Palmipedes (web-footed birds). Any attempt to modify these metabolic processes must take into consideration the specific features of lipid metabolism in birds.

First of all, de novo lipogenesis, i.e., synthesis of fatty acids, is very limited in adipose tissue and does not occur in the ovary (Saadoun and Leclercq 1987). Thus, triglyceride storage in these compartments depends on the availability of a plasma lipid substrate originating from either the diet or lipogenesis in the liver. In young broiler chickens approaching market weight, about 80–85% of the fatty acids that accumulate in the adipose tissue are derived from plasma lipids (Griffin et al. 1992). Because commercial avian breeds are usually fed lipiddoor diets (less than 10%), the liver plays a key role in providing lipids destined to be used by all tissues, including the liver itself.

Intestinal and hepatic lipids are assembled and secreted as lipoprotein particles. Extrahepatic fattening in poultry depends therefore on two successive steps of lipoprotein metabolism: 1) the level of their synthesis and secretion, and 2) their intravascular catabolism, leading to lipid uptake and storage by adipose tissue.

INTESTINAL LIPOPROTEINS

Intestinal digestion of dietary lipids, which consist essentially of triglycerides, involves their partial hydrolysis, absorption and reassembly in the intestinal mucosal cells into very large lipoprotein particles. Because the intestinal lymphatic system is poorly developed in birds, lipoproteins are secreted directly into the portal system and are therefore termed portomicrons (Bensadoun and Rothfield 1972). Their size (mean diameter of about 150 nm) and composition (about 90% triglycerides) are very similar to those of mammalian chylomicrons (Griffin et al. 1982).

Portomicrons pass through the liver before they reach the rest of the circulation. However, it is likely that these particles are too large to go through the cellular sieve of the hepatic capillary bed and are not metabolized by the liver (Fraser et al. 1986). They are absent from the plasma of unfed birds and are in very low concentration in fed immature birds. This situation reflects not only the relatively low amounts of fat in most poultry diets but also the very rapid catabolism of portomicrons in extrahepatic tissues (see below).

Lipoprotein Synthesis and Secretion in the Liver

Hepatic lipogenesis in birds. De novo fatty acid synthesis in birds, as in mammals, depends on the availability of dietary

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carbohydrate to ultimately provide acetyl-CoA and is thus enhanced in fed animals. Moreover, in animals in the fed state, insulin stimulates the activity of the main enzymes involved in lipogenesis, namely malate dehydrogenase (MD) and fatty acid synthase (FAS). The current knowledge of the hormonal and nutritional regulation of lipogenesis in growing birds has been described in a recent review by Hillgartner et al. (1995).

In laying hens, hepatic lipogenesis is dramatically enhanced by estrogens in order to meet the demand for vitellogenesis. Although the main products of de novo hepatic lipogenesis are triglycerides, the liver is also the major site of cholesterol and phospholipid synthesis. These lipids, along with protein, are the main components of lipoproteins.

**Lipoprotein synthesis.** Very low density lipoprotein and HDL are the two main classes of lipoprotein particles that are synthesized and secreted by the liver. The specific protein moieties [apolipoproteins (apo)] of these lipoprotein particles are also synthesized in the liver. Apolipoprotein B-100 (Siuta-Mangano et al. 1982) and apo A-I (Banarjee and Redman 1984) are the major apolipoproteins of chicken VLDL and HDL, respectively. With regard to VLDL, the assembly of triglycerides, phospholipids, cholesterol and apo B (together with apo VLDL-II in laying females) is a sequential process that begins in the endoplasmic reticulum and ends in the Golgi apparatus, from which nascent particles are packaged in vesicles and secreted. The entire sequence lasts less than 40 min after the initiation of apo B translation. Synthesis and secretion pathways of chicken HDL are believed to be similar to those of VLDL.

Lipid secretion is controlled, at least partly, by the residence time of lipoproteins in the intracellular compartments and also by the availability of lipid and protein moieties. However, it is not known why triglycerides are preferentially associated with apo B into VLDL particles, whereas most of the phospholipids and cholesterol are associated with apo A-I in HDL.

**Regulation of lipoprotein secretion.** Very little is known about the regulation of lipoprotein synthesis and secretion in avian liver, at least in growing birds. Fundamental work by Tarlow et al. (1977) on chicken hepatocytes demonstrated that insulin enhances both de novo lipogenesis and VLDL synthesis, whereas thyroxine and glucagon have opposite effects. In this context, the hormonal background may be very important in generating differences in rates of hepatic lipogenesis produced by genetic selection (see below). However, lipid secretion as lipoproteins may not be tightly coordinated with lipid synthesis. Indeed, in vitro studies clearly indicate that high concentrations of insulin, similar to those found in fed animals, enhance lipogenesis while inhibiting apo B synthesis. Therefore VLDL assembly and secretion is inhibited, and some triglycerides are channeled toward temporary storage into cytoplasmic vesicles (Mooney and Lane 1981).

**Lipoprotein Catabolism and Triglyceride Storage**

The transfer of triglycerides from VLDL (and portomicrons, if any) into the adipose tissue involves their catabolism by lipoprotein lipase (LPL). Lipoprotein lipase catalyses the hydrolysis of triglycerides to fatty acids and glycerol. The fatty acids then enter the surrounding tissues and, in the case of the adipose tissue, they are reesterified and stored as triglycerides. Lipoprotein lipase is synthesized in adipocytes as well as in muscle and other cell types, but only the fraction of the enzyme that has been secreted and anchored to the surface of the capillary wall is functionally active. In mammals, LPL must be activated by apo C-II, an apolipoprotein of low molecular weight that is secreted with HDL and then transferred to VLDL prior to their hydrolysis. The equivalent of apo C-II remains to be identified in birds, although it is known that HDL constitutes the major reservoir of LPL activator in chicken plasma (Griffin et al. 1982). In laying hens, the plasma catabolism of VLDL is very limited (Griffin et al. 1982), which allows the transport of lipids to oocytes, where VLDL are endocytosed, rather than to other tissues. Indeed, laying hen apo VLDL contain large amounts of apo VLDL-II, an apolipoprotein that is synthesized only under the influence of estrogen and which has been shown to be a specific inhibitor of LPL (Schneider et al. 1990).

**Regulation of lipoprotein lipase activity.** In fed mammals, LPL activity is enhanced in adipose tissue but is low in muscle, which results in fat storage. The opposite is seen in unfed animals. In birds, LPL regulation in the adipose tissue seems to be less sensitive to the nutritional state (Hermier et al. 1984). There is a paucity of information on the hormonal regulation of LPL in birds. Very high concentrations of insulin stimulate LPL activity in chicken adipose tissue (Borron et al. 1979), whereas dibutyryl cAMP can decrease both the synthesis and the activity of the enzyme in chicken adipocytes (Bensadoun and Martin 1986).

**CONTROL OF EXTRAHEPATIC FATTENING IN GROWING BIRDS VIA LIPOPROTEIN METABOLISM**

Intestinal portomicrons are usually in very low amounts, and HDL contain less than 5% triglycerides. Thus, adipose tissue growth in birds depends mainly on the availability of triglycerides transported by VLDL. Theoretically, it should be possible to alter VLDL metabolism in three compartments: liver, plasma and adipose tissue.

**VLDL synthesis and secretion.** From what is known on the role of the avian liver in lipogenesis, it may be inferred that any increase in hepatic fatty acid synthesis should lead to a higher lipid secretion. Indeed, in growing chickens, the activities of MD and ATP citrate lyase, which are both involved in fatty acid synthesis, have shown positive correlations (0.4–0.5) with body fatness [high (H)-VLDL and low (L)-VLDL lines; Whitehead et al. 1984]. This hypothesis has been tested on chickens selected for leanness and fatness on either abdominal fat content at 9 wk (lean and fat lines; Leclercq et al. 1980) or plasma VLDL concentration at 7 wk (H-VLDL and L-VLDL lines; Whitehead and Griffin 1984) (Table 1, and see below). Hepatic lipogenesis was estimated via the incorporation of tritiated water and was found to be higher in the fat line rather than in the lean line (Saadoun and Leclercq 1987), whereas H-VLDL and L-VLDL chickens exhibited no consistent differences (Asante and Griffin 1988). In the latter lines, Bannister et al. (1984) found that the activities of enzymes involved in fatty acid synthesis in birds, such as FAS, MD and ATP citrate lyase, were significantly higher in the liver of fat H-VLDL chickens. In contrast, the differences in the activity of MD were not significant between fat and lean chickens (Asante and Bulfeld 1988). However, as compared with lean birds, fat chickens exhibited a significantly higher hepatic Δ9 desaturase activity, which is thought to facilitate the incorporation of fatty acids into VLDL and their subsequent secretion towards extrahepatic tissues (Legrand et al. 1987). Very low density lipoprotein secretion was also deter-
LIPROTEIN METABOLISM AND FATTENING

TABLE 1

Anatomic and metabolic changes in fat chickens compared with their lean counterparts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Abdominal fat content</th>
<th>Plasma VLDL concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight</td>
<td>No difference (Leclercq et al. 1980)</td>
<td>No difference (Whitehead 1988)</td>
</tr>
<tr>
<td>Food intake</td>
<td>No difference (Leclercq et al. 1980)</td>
<td>No difference (Whitehead 1988)</td>
</tr>
<tr>
<td>Abdominal fat content</td>
<td>Increased (Leclercq et al. 1980)</td>
<td>Increased (Whitehead and Griffin 1984)</td>
</tr>
<tr>
<td>Adipocyte size</td>
<td>Increased (Hermier et al. 1989)</td>
<td>ND1</td>
</tr>
<tr>
<td>Adipocyte number</td>
<td>Increased (Hermier et al. 1989)</td>
<td>ND</td>
</tr>
<tr>
<td>Hepatic lipogenesis</td>
<td>Increased (Saadoun and Leclercq 1987)</td>
<td>No difference (Asante and Griffin 1988)</td>
</tr>
<tr>
<td>NADPH-generating enzymes</td>
<td>No difference (Asante and Buffield 1988)</td>
<td>Increased (Bannister et al. 1984)</td>
</tr>
<tr>
<td>ΔS-Desaturase</td>
<td>Increased (Legrand et al. 1987)</td>
<td>ND</td>
</tr>
<tr>
<td>VLDL secretion</td>
<td>Increased (Leclercq et al. 1980)</td>
<td>Increased (Griffin et al. 1989)</td>
</tr>
<tr>
<td>VLDL concentration</td>
<td>Increased (Hermier et al. 1984)</td>
<td>Increased (Whitehead and Griffin 1984)</td>
</tr>
<tr>
<td>LPL/abdominal fat pad</td>
<td>Increased (Hermier et al. 1989)</td>
<td>No difference (Griffin et al. 1989)</td>
</tr>
<tr>
<td>LPL/adipocyte</td>
<td>No difference (Hermier et al. 1989)</td>
<td>ND</td>
</tr>
</tbody>
</table>

1ND = not determined.

minded directly after inhibition of LPL in H-VLDL and L-VLDL chickens (Griffin et al. 1989) as well as in lean and fat chickens (Leclercq et al. 1990). In both studies, plasma VLDL accumulation was considerably higher in the fat line.

Taken together, these data suggest that fattening results, at least partly, from an increased hepatic lipogenesis. However, all previous studies failed to find any enzymatic criterion that could be usable in a selection program against fatness in broilers. This is probably due to the fact that, in the daily conditions encountered in poultry production, enzymatic activities in the liver are not a limiting factor of lipogenesis and VLDL synthesis.

**Plasma VLDL concentration.** When determined in lean and fat chickens, the plasma concentration of VLDL was two-fold higher in the fat line (Hermier et al. 1984), which indicated that VLDL concentration reflected the availability of plasma triglycerides and therefore the susceptibility to fattening, in accordance with previous studies (Whitehead and Griffin 1982). As a consequence, divergent selection for plasma VLDL level resulted in two lines with a sixfold difference in plasma VLDL and a threefold difference in the relative abdominal fat pad weight (Whitehead and Griffin 1984).

It is noteworthy that, in the comparison of lean and fat chickens, and whatever the selection criterion, differences found in hepatic lipogenesis or activity of lipogenic enzymes are much smaller than the accompanying differences in plasma VLDL concentrations and are often not significant. Serum turbidity, a reflection of VLDL concentration, can be determined rather easily from blood samples, which allows direct selection (Whitehead and Griffin 1982 and 1984). Thus, this variable has been included in selection programs against excessive fattening of broilers in Great Britain.

Selection for leanness on the basis of plasma VLDL should be also applicable to other avian species that show continuous patterns of feeding. This is the case in turkeys, in which VLDL concentration was a good indicator of the degree of fattiness (Griffin and Whitehead 1985). This is also in accordance with the results of Kouba et al. (1995), who showed that at the same age and similar body weight, the 80% lower proportion of the abdominal adipose tissue in turkeys compared with chickens was associated with a 85% lower plasma VLDL concentration.

**VLDL catabolism.** Lipoprotein lipase is the rate-limiting enzyme in the hydrolysis of plasma triglyceride-rich lipoproteins. However, there is no experimental evidence that LPL activity is a determining factor in the regulation of fattening in birds. In fact, positive correlations were found between adipose tissue LPL activity and growth of fat depots in broilers (Griffin et al. 1987), but this does not prove that fatness results from higher LPL activity. More likely, LPL activity increases with the number of adipocytes and thus reflects the degree of hyperplasia, rather than an increase in the fat-storing ability of individual cells per se. Indeed, fat chickens selected on the basis of their abdominal fat content exhibited a dramatic adipocyte hyperplasia. Consequently, in these birds compared with lean chickens, abdominal fat pad and LPL activity/pad were fourfold higher, whereas LPL activity per cell did not differ between lean and fat lines (Hermier et al. 1989).

In lean and fat chickens selected according to plasma VLDL concentration, LPL activity of the whole abdominal fat pad was found to be similar and thus could not account for the different susceptibility to fattening. However, LPL activity was higher in various muscles (including the heart) of lean L-VLDL chickens (Griffin et al. 1989). This is in accordance with the preferential use of VLDL-triglyceride for oxidation in the muscle rather than for adipose storage (Griffin et al. 1992).

Selection for low LPL activity should result in a reduction in the number of adipocytes, as well as a decreased propensity for fat storage. However, for practical purposes, LPL is not a good criterion, because the determination and expression of LPL activity cannot be routinely performed, and a biopsy sample may not be representative of whole-body activity.

**LIVER STEATOSIS**

Fatty liver occurs in birds when the increase in lipogenesis exceeds the capacity of synthesis and secretion of lipoproteins. This is the case in laying females, in which the dramatic enhancement of lipogenesis by estrogen is responsible for an increase in VLDL secretion. In certain instances, the latter can be not sufficient to prevent the occurrence of a metabolic disease of laying hens known as fatty liver hemorrhagic syndrome (Hansen and Walzem 1993). The disease generally results in reduced egg production and increased mortality.

The wild Palmipedes develop a general fattening before their migration, and the fatty liver spontaneously serves as an energy storage organ. This natural ability to store energy is used for the production of “foie-gras” by overfeeding specific breeds of ducks and geese with a carbohydrate-rich diet. Under these conditions, hepatic lipogenesis is dramatically enhanced,
and the liver weight may increase from 100 g to 1 kg in 2 wk (Hermier et al. 1994). Liver steatosis is due to a specific accumulation of triglycerides within the parenchymal cells, the mechanism of which remains poorly understood. In geese, overfeeding leads to a dramatic increase in VLDL and HDL concentrations. However, these VLDL contain less triglycerides (29–35% vs. 43% in control goose), indicating that a defect in the incorporation of triglycerides into nascent VLDL particles may be responsible for the hepatic fat accumulation in this species (Hermier et al. 1994). The reason why neosynthetised triglycerides are channeled towards intracytoplasmic storage rather than secretion remains unclear. In fed chickens, considerable amounts of triglycerides are temporarily stored by the liver but need a further hydrolysis and reesterification before they can enter the secretion pathway (Mooney and Lane 1981). It is possible that, because the overfed geese are never deprived of food, hormonal regulation does not allow the liver to secrete the excess of triglycerides, which continue to accumulate.

CONCLUSION

Extrahepatic fattening in birds seems to result from an increased lipogenesis, leading to an enhanced production of VLDL; VLDL are then catabolized by what seems to be a substrate-rate process, whereas LPL does not seem to be a limiting factor. A preexisting adipocyte hyperplasia is an aggravating factor that allows an increased fat storage.

Differences between genetically lean and fat chickens are by nature polygenic, and it is obvious that propensity to leanness or fatness in poultry relies on fundamental metabolic molecular mechanisms involved in nutritional regulation of fatty acid synthesis. In particular, the control of VLDL production. Nutritional at

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